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10/604,400	07/17/2003	Eric T. KOOL	12665.0024.NPUS01	1399

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EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/604,400	KOOL, ERIC T.	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-49* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-16 and 40-49, drawn to a composition comprising a fluorophore compound comprising a fluorophore group and a fluorescence quenching group, classified in class 536, subclass 24.3, for example.

II. Claims 17-24, drawn to a method of detecting intramolecular chemical ligation, the method comprising:

providing a composition comprising a fluorophore compound, wherein the compound comprises a fluorophore group, a fluorescence quenching leaving group, and a nucleophilic group;

maintaining the composition under conditions suitable for intramolecular chemical ligation; and

determining the fluorescence of the composition, classified in class 435, subclass 91.5, for example.

III. Claims 25-39, drawn to a method of detecting a nucleic acid sequence of interest, the method comprising:

providing a nucleic acid molecule suspected of comprising a nucleic sequence of interest;

providing a first nucleic acid probe that hybridizes to at least a portion of the nucleic acid sequence of interest;

providing a second nucleic acid probe that hybridizes to at least a portion of the nucleic acid sequence of interest adjacent to the first nucleic acid probe;

combining the nucleic acid molecule, the first nucleic acid probe, and the second nucleic acid probe to form a mixture;

maintaining the mixture under conditions suitable for hybridization of the first nucleic acid probe and the second nucleic acid probe to the nucleic acid molecule; and, determining the fluorescence of the mixture; wherein:

the first nucleic acid probe comprises a fluorophore group and a fluorescence quenching leaving group;

the second nucleic acid probe comprises a nucleophilic group; and

when the first nucleic acid probe and the second nucleic acid probe hybridize to the nucleic acid molecule, the nucleophilic group can displace the fluorescence quenching leaving group, classified in class 435, subclass 6, for example.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and (II and III) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the fluorophore compound of Group I can be used to detect changes in the active site of protein on binding of an analyte rather than in the methods of Groups II and III.

Searching the inventions of Groups I and (II and III) together would impose serious search burden. The inventions of Groups I and (II and III) have a separate status in the art as shown by their different classifications. Moreover, in the instant case, the search for the fluorophore compound and the methods of detecting intramolecular chemical ligation or nucleic acid sequence using a fluorophore compound are not coextensive. Group I encompasses molecules belong to any

classes of molecules which are labeled with fluorophore and a quencher, which are not required for the search of Groups II and III. In contrast, the search for group II would require a search for the method of detecting intramolecular chemical ligation, and the method of Group III requires search for nucleic acids labeled with fluorophores and quenchers. Prior art which teaches a fluorophore compound of Group I would not necessarily be applicable to the method of using the fluorophore compound. Moreover, even if the fluorophore compound were known, the method of using the product may be novel and unobvious in view of the preamble or active steps.

3. Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed to methods with different materials, method steps and goals.

The method of detecting intramolecular chemical ligation (group II) and the method of detecting a nucleic acid sequence of interest (group III) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using a structurally and functionally divergent material. Moreover, the methodology and materials necessary for detecting intramolecular chemical ligation and detecting a nucleic acid sequence of interest differ significantly for each of the materials, as the intramolecular ligation reaction can be accomplished using two different chemical compounds, two peptides or proteins, or a small molecule and nucleic acid, peptide or carbohydrate, whereas the method of Group III is accomplished using nucleic acid molecules. Therefore, each method is divergent in steps and goals as well as in the materials used. For these reasons the Inventions II and III are patentably distinct.

Furthermore, the distinct steps and products require separate and distinct searches. The inventions of Groups II and III have a separate status in the art as shown by their different classifications. As such, it would be burdensome to search the inventions of Groups II and III together.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

5. This application contains claims directed to the following patentably distinct species of the claimed invention:

Group I

Species of the fluorophore compound

A) fluorophore compound is an organic compound (claim 5, in part),

B) fluorophore compound is an organometllic compound (claim 5, in part),

C) fluorophore compound is a nucleic acid (claim 5, in part, claims 6-11),

D) fluorophore compound is a peptide (claims 5 and 16, in part),

E) fluorophore compound is a protein (claims 5 and 16, in part),

F) fluorophore compound is a lipid (claim 5, in part),

G) fluorophore compound is a carbohydrate (claim 5, in part).

Species of the relationship between the fluorescence quenching group and the nucleophilic group

A) the fluorescence quenching group is attached to the 5' end of the first nucleic acid probe and the nucleophilic group is attached to the 3' end of the second nucleic acid probe (claim 41),

B) the fluorescence quenching group is attached to the 3' end of the first nucleic acid probe and the nucleophilic group is attached to the 5' end of the second nucleic acid probe (claim 42).

Species of the relationship between the fluorescence quenching group and the fluorophore group

A) the fluorescence quenching group is attached to the first nucleic acid probe one nucleotide away from the fluorophore group (claim 43),

B) the fluorescence quenching group is attached to the first nucleic acid probe two nucleotides away from the fluorophore group (claim 44),

C) the fluorescence quenching group is attached to the first nucleic acid probe three nucleotides away from the fluorophore group (claim 45).

Group III

Species of the relationship between the fluorescence quenching group and the nucleophilic group

A) the fluorescence quenching group is attached to the 5' end of the first nucleic acid probe and the nucleophilic group is attached to the 3' end of the second nucleic acid probe (claim 26),

B) the fluorescence quenching group is attached to the 3' end of the first nucleic acid probe and the nucleophilic group is attached to the 5' end of the second nucleic acid probe (claim 27, 28).

Species of the relationship between the fluorescence quenching group and the fluorophore group

A) the fluorescence quenching group is attached to the first nucleic acid probe one nucleotide away from the fluorophore group (claim 29),

B) the fluorescence quenching group is attached to the first nucleic acid probe two nucleotides away from the fluorophore group (claim 30),

C) the fluorescence quenching group is attached to the first nucleic acid probe three nucleotides away from the fluorophore group (claim 31).

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 25 and 40 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. For example, if Group I is selected, Applicant should elected one species from the group of fluorophore compounds, one from the group of relationship between quenching groups and nucleophilic groups and one species from the group of relationship between quenching groups and fluorophores. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

7. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TERESA STRZELECKA
PATENT EXAMINER
Teresa Strzelecka
1/8/06